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Name

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Attorney Docket No. 01-1693-F)  
(previously 13615.21USU1)

In re Application of:	)	
	)	
Fang et al.	)	
	)	Before the Examiner:
Serial No.: 09/895,871	)	Richard L. Raymond
	)	
Filed: June 29, 2001	)	Art Unit: 1624
	)	
For: Compounds to Treat	)	
Alzheimer's Disease	)	Confirmation No.: 5372

RESPONSE TO THE OFFICE ACTION  
MAILED JUNE 12, 2003

Mail Stop Patent Ext.  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Responsive to the Office Action mailed January 13, 2003, Applicants respectfully request the Examiner to reconsider the above-identified patent application in view of the following

Amendments	and	Remarks.
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- $$\begin{array}{c}
 \text{OH} \\
 | \\
 \text{R}_N - \text{N} - \text{CH} - \text{C} - \text{NH} - \text{R}_C \\
 | \quad | \quad | \quad | \\
 \text{H} \quad \text{R}_1 \quad \text{R}_2 \quad \text{R}_3
 \end{array} \quad (\text{X})$$

~~(II)  $\text{CH}_2\text{-S(O)}_{0-2}\text{-(C}_1\text{-C}_6\text{-alkyl)}$ ,~~  
~~(III)  $\text{CH}_2\text{-CH}_2\text{-S(O)}_{0-2}\text{-(C}_1\text{-C}_6\text{-alkyl)}$ ,~~  
~~(IV)  $\text{C}_2\text{-C}_6\text{-alkenyl}$  with one or two double bonds,  
optionally substituted with one, two or three substituents  
selected from the group consisting of F, Cl, OH, SH,  $\text{C}\equiv\text{N}$ ,  
 $\text{CF}_3$ ,  $\text{C}_1\text{-C}_2\text{-alkoxy}$ , and  $\text{NR}_{1-2}\text{R}_{1-2}$  where  $\text{R}_{1-2}$  and  $\text{R}_{1-2}$  are H or  $\text{C}_1\text{-C}_6$   
alkyl,~~  
~~(V)  $\text{C}_2\text{-C}_6\text{-alkynyl}$  with one or two triple bonds,  
optionally substituted with one, two or three substituents  
selected from the group consisting of F, Cl, OH, SH,  $\text{C}\equiv\text{N}$ ,  
 $\text{CF}_3$ ,  $\text{C}_1\text{-C}_2\text{-alkoxy}$ , and  $\text{NR}_{1-2}\text{R}_{1-2}$  where  $\text{R}_{1-2}$  and  $\text{R}_{1-2}$  are H or  $\text{C}_1\text{-C}_6$   
alkyl,~~  
(VI)  $\text{-(CH}_2\text{)}_{n_1}\text{-(R}_{1\text{-aryl}}\text{)}$  where  $n_1$  is zero or one and where  
 $\text{R}_{1\text{-aryl}}$  is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl,

~~dihydronaphthyl, or tetralinyl~~ optionally substituted with one, two, three or four of the following substituents on the aryl ring:

(A) C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

A<sup>1</sup>  
(B) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(D) -F, Cl, -Br, or -I,

(E) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three -F,

(F) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(G) -OH,

(H) -C≡N,

(I) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(J) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(K) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(L)  $-\text{CO}-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above, or

(M)  $-\text{SO}_2-(\text{C}_1-\text{C}_4 \text{ alkyl}),$

~~(VII)  $(\text{CH}_2)_{n_1}(\text{R}_{1\text{-heteroaryl}})$  where  $n_1$  is as defined above and where  $\text{R}_{1\text{-heteroaryl}}$  is selected from the group consisting of:~~

~~pyridinyl,~~  
~~pyrimidinyl,~~  
~~quinolinyl,~~  
~~benzothienyl,~~  
~~indolyl,~~  
~~indolinyl,~~  
~~pyridazinyl,~~  
~~pyrazinyl,~~  
~~isoindolyl,~~  
~~isquinolyl,~~  
~~quinazolinyl,~~  
~~quinexalinyl,~~  
~~phthalazinyl,~~  
~~imidazolyl,~~  
~~isoxazolyl,~~  
~~pyrazolyl,~~  
~~oxazolyl,~~  
~~thiazolyl,~~  
~~indolizinyll,~~  
~~indazolyl,~~  
~~benzothiazolyl,~~  
~~benzimidazolyl,~~  
~~benzofuranyl,~~  
~~furanyl,~~  
~~thienyl,~~  
~~pyrrolyl,~~  
~~oxadiazolyl,~~

Al

~~thiadiazolyl,~~  
~~triazolyl,~~  
~~tetrazolyl,~~  
~~oxazolopyridinyl,~~  
~~imidazopyridinyl,~~  
~~isothiazolyl,~~  
~~naphthyridinyl,~~  
~~cinnolinyl,~~  
~~carbazolyl,~~  
~~beta-carbolinyl,~~  
~~isochromanlyl,~~  
~~chromanlyl,~~  
~~tetrahydroisoquinolinyl,~~  
~~isoindolinyl,~~  
~~isobenzotetrahydrofuranlyl,~~  
~~isobenzotetrahydrothienyl,~~  
~~isobenzothienyl,~~  
~~benzoxazolyl,~~  
~~pyridopyridinyl,~~  
~~benzotetrahydrofuranlyl,~~  
~~benzotetrahydrothienyl,~~  
~~purinyl,~~  
~~benzodioxolyl,~~  
~~triazinyl,~~  
phenoxazinyl,  
phenothiazinyl,  
pteridinyl,  
benzothiazolyl,  
imidazopyridinyl,  
imidazethiazolyl,  
dihydrobenzisoxazinyl,  
benzisoxazinyl,

benzoxazinyl,  
dihydrobenzisothiazinyl,  
benzopyranyl,  
benzothiopyranyl,  
coumarinyl,  
isocoumarinyl,  
chromenyl,  
chromanonyl,  
pyridinyl N-oxide  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisquinolinonyl  
dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
pyrrolyl N-oxide,  
pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
indolyl N-oxide,  
indolinyl N-oxide,  
isquinolyl N-oxide,  
quinazolinyl N-oxide,  
quinoxalinyl N-oxide,  
phthalazinyl N-oxide,  
imidazolyl N-oxide,  
isoxazolyl N-oxide,  
oxazolyl N-oxide,

thiazolyl N-oxide,  
indoliziny N-oxide,  
indazolyl N-oxide,  
benzothiazolyl N-oxide,  
benzimidazolyl N-oxide,  
pyrrolyl N-oxide,  
oxadiazolyl N-oxide,  
thiadiazolyl N-oxide,  
triazolyl N-oxide,  
tetrazolyl N-oxide,  
benzothiopyranyl S-oxide, and  
benzothiopyranyl S,S-dioxide,

where the  $R_1$ -heteroaryl group is bonded to  $(CH_2)_{n1}$  by any ring atom of the parent  $R_1$ -heteroaryl group substituted by hydrogen such that the new bond to the  $R_1$ -heteroaryl group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three or four of:

(1)  $C_1$ - $C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1$ - $C_3$  alkyl, F, Cl, Br, I, OH, SH, C=N,  $CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $NR_{1a}R_{1b}$  where  $R_{1a}$  and  $R_{1b}$  are as defined above,

(2)  $C_2$ - $C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of F, Cl, OH, SH, C=N,  $CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $NR_{1a}R_{1b}$  where  $R_{1a}$  and  $R_{1b}$  are H or  $C_1$ - $C_6$  alkyl,

(3)  $C_2$ - $C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of F, Cl, OH, SH, C=N,

~~CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are H or C<sub>1</sub>-C<sub>6</sub> alkyl,~~

~~(4) F, Cl, Br, or I,~~

~~(5) C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three F,~~

~~(6) NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined below,~~

~~(7) OH,~~

~~(8) C≡N,~~

~~(9) C<sub>3</sub>-C<sub>6</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of F, Cl, OH, SH, C≡N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>2</sub> alkoxy, and NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are H or C<sub>1</sub>-C<sub>6</sub> alkyl,~~

~~(10) CO (C<sub>1</sub>-C<sub>4</sub> alkyl),~~

~~(11) SO<sub>2</sub> NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined above,~~

~~(12) CO NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined above,~~

~~(13) SO<sub>2</sub> (C<sub>1</sub>-C<sub>4</sub> alkyl), with the proviso that when n<sub>1</sub> is zero R<sub>1-heterocycle</sub> is not bonded to the carbon chain by nitrogen,~~

~~(VIII) (CH<sub>2</sub>)<sub>n1</sub> (R<sub>1-heterocycle</sub>) where n<sub>1</sub> is as defined above and R<sub>1-heterocycle</sub> is selected from the group consisting of~~

~~morpholinyl,~~

~~thiomorpholinyl,~~

~~thiomorpholinyl S-oxide,~~

~~thiomorpholinyl S,S-dioxide,~~

~~piperazinyl,~~

~~homopiperazinyl,~~

~~pyrrolidinyl,~~

~~pyrrolinyl,~~



~~tetrahydropyranyl,~~  
~~piperidinyl,~~  
~~tetrahydrofuranyl,~~  
~~tetrahydrothienyl,~~  
~~homopiperidinyl,~~  
~~homomorpholinyl,~~  
~~homothiomorpholinyl,~~  
~~homothiomorpholinyl S,S-dioxide,~~  
~~oxazolidinonyl,~~  
~~dihydropyrazolyl,~~  
~~dihydropyrrolyl,~~  
~~dihydropyrazinyl,~~  
~~dihydropyridinyl,~~  
~~dihydropyrimidinyl,~~  
~~dihydrofuryl,~~  
~~dihydropyranyl,~~  
~~tetrahydrothienyl S-oxide,~~  
~~tetrahydrothienyl S,S-dioxide, and~~  
~~homothiomorpholinyl S-oxide,~~

where the ~~R<sub>1</sub> heterocycle~~ group is bonded by any atom of the parent ~~R<sub>1</sub> heterocycle~~ group substituted by hydrogen such that the new bond to the ~~R<sub>1</sub> heterocycle~~ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three or four:

(1) ~~C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, F, Cl, Br, I, OH, SH, C=N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined above,~~

(2) ~~C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three~~

~~substituents selected from the group consisting of F, Cl, OH, SH, C=N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub>-alkoxy, and NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are H or C<sub>1</sub>-C<sub>6</sub>-alkyl,~~

~~(3) C<sub>3</sub>-C<sub>6</sub>-alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of F, Cl, OH, SH, C=N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>2</sub>-alkoxy, and NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are H or C<sub>1</sub>-C<sub>6</sub>-alkyl,~~

~~(4) F, Cl, Br, or I,~~

~~(5) C<sub>1</sub>-C<sub>6</sub>-alkoxy optionally substituted with one, two, or three F,~~

~~(6) NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined below,~~

~~(7) OH,~~

~~(8) C=N,~~

~~(9) C<sub>3</sub>-C<sub>6</sub>-cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of F, Cl, OH, SH, C=N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>2</sub>-alkoxy, and NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are H or C<sub>1</sub>-C<sub>6</sub>-alkyl,~~

~~(10) CO (C<sub>1</sub>-C<sub>4</sub>-alkyl),~~

~~(11) SO<sub>2</sub> NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined above,~~

~~(12) CO NR<sub>1a</sub>R<sub>1b</sub> where R<sub>1a</sub> and R<sub>1b</sub> are as defined above,~~

~~(13) SO<sub>2</sub> (C<sub>1</sub>-C<sub>4</sub>-alkyl),~~

~~(14) O, with the proviso that when n<sub>1</sub> is zero R<sub>1</sub>-heterocycle is not bonded to the carbon chain by nitrogen, where R<sub>2</sub> is:~~

(I) -H, or

(II)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>,  $C_1-C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above;

where R<sub>3</sub> is:

(I) -H, or

(II)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>,  $C_1-C_3$  alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above;

and where R<sub>2</sub> and R<sub>3</sub> are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO<sub>2</sub>-, and -NR<sub>N-2</sub>-, where R<sub>N-2</sub> is as defined below;

where R<sub>N</sub> is:

(I) R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is ~~selected from the group consisting of:~~

~~(A) -CO-, and~~

~~(B) -SO<sub>2</sub>-~~

where R<sub>N-1</sub> is selected from the group consisting of:

~~(A) R<sub>N-aryl</sub> where R<sub>N-aryl</sub> is phenyl, 1-naphthyl, 2-naphthyl, tetralinyl, indanyl, dihydronaphthyl or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, optionally substituted with one, two or three of the following substituents which can be the same or different and are:~~

(1) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2) -OH,

(3) -NO<sub>2</sub>,

(4) -F, -Cl, -Br, or -I,

(5) -CO-OH,

(6) -C≡N,

(7) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are selected from the group consisting of:

(a) -H,

(b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one ~~substituent~~ substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH<sub>2</sub>,

(c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,

(d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),

(g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

(h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,

(i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,

(j)  $-R_1\text{-aryl}$  where  $R_1\text{-aryl}$  is as defined above, and

(k)  $-R_1\text{-heteroaryl}$  where  $R_1\text{-heteroaryl}$  is as defined above,

(8)  $-(CH_2)_{0-4}\text{-CO-}(C_1\text{-}C_{12}\text{ alkyl})$ ,

(9)  $-(CH_2)_{0-4}\text{-CO-}(C_2\text{-}C_{12}\text{ alkenyl with one, two or three double bonds})$ ,

(10)  $-(CH_2)_{0-4}\text{-CO-}(C_2\text{-}C_{12}\text{ alkynyl with one, two or three triple bonds})$ ,

(11)  $-(CH_2)_{0-4}\text{-CO-}(C_3\text{-}C_7\text{ cycloalkyl})$ ,

(12)  $-(CH_2)_{0-4}\text{-CO-}R_1\text{-aryl}$  where  $R_1\text{-aryl}$  is as defined above,

(13)  $-(CH_2)_{0-4}\text{-CO-}R_1\text{-heteroaryl}$  where  $R_1\text{-heteroaryl}$  is as defined above,

(14)  $-(CH_2)_{0-4}\text{-CO-}R_1\text{-heterocycle}$  where  $R_1\text{-heterocycle}$  is as defined above,

(15)  $-(CH_2)_{0-4}\text{-CO-}R_{N-4}$  where  $R_{N-4}$  is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of  $C_1\text{-}C_6$  alkyl,

(16)  $-(CH_2)_{0-4}\text{-CO-O-}R_{N-5}$  where  $R_{N-5}$  is selected from the group consisting of:

(a)  $C_1\text{-}C_6$  alkyl,

(b)  $-(CH_2)_{0-2}\text{-(}R_1\text{-aryl)}$  where  $R_1\text{-aryl}$  is as defined above,

(c)  $C_2\text{-}C_6$  alkenyl containing one or two double bonds,

(d)  $C_2\text{-}C_6$  alkynyl containing one or two triple bonds,

(e)  $C_3\text{-}C_7$  cycloalkyl,

(f) -  $(\text{CH}_2)_{0-2} - (\text{R}_1\text{-heteroaryl})$  where  $\text{R}_1\text{-heteroaryl}$  is as defined above,

(17) -  $(\text{CH}_2)_{0-4} - \text{SO}_2 - \text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are as defined above,

(18) -  $(\text{CH}_2)_{0-4} - \text{SO} - (\text{C}_1\text{-C}_8 \text{ alkyl})$ ,

(19) -  $(\text{CH}_2)_{0-4} - \text{SO}_2 - (\text{C}_1\text{-C}_{12} \text{ alkyl})$ ,

(20) -  $(\text{CH}_2)_{0-4} - \text{SO}_2 - (\text{C}_3\text{-C}_7 \text{ cycloalkyl})$ ,

(21) -  $(\text{CH}_2)_{0-4} - \text{N}(\text{H or R}_{\text{N}-5}) - \text{CO} - \text{O} - \text{R}_{\text{N}-5}$  where  $\text{R}_{\text{N}-5}$  can be the same or different and is as defined above,

(22) -  $(\text{CH}_2)_{0-4} - \text{N}(\text{H or R}_{\text{N}-5}) - \text{CO} - \text{N}(\text{R}_{\text{N}-5})_2$ , where  $\text{R}_{\text{N}-5}$  can be the same or different and is as defined above,

(23) -  $(\text{CH}_2)_{0-4} - \text{N} - \text{CS} - \text{N}(\text{R}_{\text{N}-5})_2$ , where  $\text{R}_{\text{N}-5}$  can be the same or different and is as defined above,

(24) -  $(\text{CH}_2)_{0-4} - \text{N}(-\text{H or R}_{\text{N}-5}) - \text{CO} - \text{R}_{\text{N}-2}$  where  $\text{R}_{\text{N}-5}$  and  $\text{R}_{\text{N}-2}$  can be the same or different and are as defined above,

(25) -  $(\text{CH}_2)_{0-4} - \text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  can be the same or different and are as defined above,

(26) -  $(\text{CH}_2)_{0-4} - \text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,

(27) -  $(\text{CH}_2)_{0-4} - \text{O} - \text{CO} - (\text{C}_1\text{-C}_6 \text{ alkyl})$ ,

(28) -  $(\text{CH}_2)_{0-4} - \text{O} - \text{P}(\text{O}) - (\text{OR}_{\text{N-aryl-1}})_2$  where  $\text{R}_{\text{N-aryl-1}}$  is -H or  $\text{C}_1\text{-C}_4 \text{ alkyl}$ ,

(29) -  $(\text{CH}_2)_{0-4} - \text{O} - \text{CO} - \text{N}(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(30) -  $(\text{CH}_2)_{0-4} - \text{O} - \text{CS} - \text{N}(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(31) -  $(\text{CH}_2)_{0-4} - \text{O} - (\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(32) -  $(\text{CH}_2)_{0-4} - \text{O} - (\text{R}_{\text{N}-5})_2 - \text{COOH}$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(33) -  $(\text{CH}_2)_{0-4} - \text{S} - (\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,

(34)  $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl optionally substituted with one, two, three, four, or five } -F)$ ,

(35)  $C_3-C_7 \text{ cycloalkyl}$ ,

(36)  $C_2-C_6 \text{ alkenyl with one or two double bonds optionally substituted with } C_1-C_3 \text{ alkyl, } -F, -Cl, -Br, -I, -OH, -SH, -C\equiv N, -CF_3, C_1-C_3 \text{ alkoxy, and } -NR_{1-a}R_{1-b} \text{ where } R_{1-a} \text{ and } R_{1-b} \text{ are as defined above,}$

A' (37)  $C_2-C_6 \text{ alkynyl with one or two triple bonds optionally substituted with } C_1-C_3 \text{ alkyl, } -F, -Cl, -Br, -I, -OH, -SH, -C\equiv N, -CF_3, C_1-C_3 \text{ alkoxy, } -NR_{1-a}R_{1-b} \text{ where } R_{1-a} \text{ and } R_{1-b} \text{ are as defined above,}$

(38)  $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$  where  $R_{N-5}$  and  $R_{N-2}$  can be the same or different and are as described above, or

(39)  $-(CH_2)_{0-4}-C_3-C_7 \text{ cycloalkyl}$ ,

~~(D)  $R_N \text{ heteroaryl}$  where  $R_N \text{ heteroaryl}$  is selected from the group consisting of:~~

~~pyridinyl,  
pyrimidinyl,  
quinolinyl,  
benzothienyl,  
indolyl,  
indolinyl,  
pyridazinyl,  
pyrazinyl,  
isoindolyl,  
isoquinolyl,  
quinazolinyl,  
quinoxalinyll,  
phthalazinyl,  
imidazolyl,~~

~~isoxazolyl,~~  
~~pyrazolyl,~~  
~~oxazolyl,~~  
~~thiazolyl,~~  
~~indolizinylyl,~~  
~~indazolyl,~~  
~~benzothiazolyl,~~  
~~benzimidazolyl,~~  
~~benzofuranyl,~~  
~~furanyl,~~  
~~thienyl,~~  
~~pyrrolyl,~~  
~~oxadiazolyl,~~  
~~thiadiazolyl,~~  
~~triazolyl,~~  
~~tetrazolyl,~~  
~~oxazolopyridinyl,~~  
~~imidazopyridinyl,~~  
~~isothiazolyl,~~  
~~naphthyridinyl,~~  
~~cinnolinyl,~~  
~~carbazolyl,~~  
~~beta-carbolinyl,~~  
~~isochromanyl,~~  
~~chromanyl,~~  
~~tetrahydroisoquinolinyl,~~  
~~isoindolinyl,~~  
~~isobenzotetrahydrofuranlyl,~~  
~~isobenzotetrahydrothienyl,~~  
~~isobenzothienyl,~~  
~~benzoxazolyl,~~  
~~pyridopyridinyl,~~



~~benzotetrahydrofuranyl,~~  
~~benzotetrahydrothienyl,~~  
~~purinyl,~~  
~~benzodioxolyl,~~  
~~triazinyl,~~  
~~hexazinyl,~~  
~~phenothiazinyl,~~  
~~pteridinyl,~~  
~~benzothiazolyl,~~  
~~imidazopyridinyl,~~  
~~imidazothiazolyl,~~  
~~dihydrobenzisoxazinyl,~~  
~~benzisoxazinyl,~~  
~~benzoxazinyl,~~  
~~dihydrobenzisoethiazinyl,~~  
~~benzopyranyl,~~  
~~benzothiopyranyl,~~  
~~coumarinyl,~~  
~~isocoumarinyl,~~  
~~chromonyl,~~  
~~chromanonyl,~~  
~~pyridinyl-N-oxide,~~  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisquinolinonyl  
dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
pyrrolyl-N-oxide,

pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
indolyl N-oxide,  
indolinyl N-oxide,  
isoquinolyl N-oxide,  
quinazolinyl N-oxide,  
quinoxalinyl N-oxide,  
phthalazinyl N-oxide,  
imidazolyl N-oxide,  
isoxazolyl N-oxide,  
oxazolyl N-oxide,  
thiazolyl N-oxide,  
indoliziny N-oxide,  
indazolyl N-oxide,  
benzothiazolyl N-oxide,  
benzimidazolyl N-oxide,  
pyrrolyl N-oxide,  
oxadiazolyl N-oxide,  
thiadiazolyl N-oxide,  
triazolyl N-oxide,  
tetrazolyl N-oxide,  
benzothiopyranyl S-oxide, and  
benzothiopyranyl S,S-dioxide,

where the ~~R<sub>N</sub> heteroaryl~~ group is bonded by any atom of the parent ~~R<sub>N</sub> heteroaryl~~ group substituted by hydrogen such that the new bond to the ~~R<sub>N</sub> heteroaryl~~ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:

(1) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group

consisting of  $C_1$ - $C_3$  alkyl, F, Cl, Br, I, OH, SH,  $C\equiv N$ ,  $CF_3$ ,  $C_1$ - $C_3$  alkoxy, and  $NR_{1.2}R_{1.3}$  where  $R_{1.2}$  and  $R_{1.3}$  are as defined above,

(2) OH,

(3)  $NO_2$ ,

(4) F, Cl, Br, I,

(5) COOH,

(6)  $C\equiv N$ ,

(7)  $-(CH_2)_{0-4}-CO-NR_{1.2}R_{1.3}$  where  $R_{1.2}$  and  $R_{1.3}$  are the same or different and are selected from the group consisting of:

(a) H,

(b)  $C_1$ - $C_6$  alkyl optionally substituted with one substituent selected from the group consisting of:

(i) OH, and

(ii)  $NH_2$ ,

(c)  $C_1$ - $C_6$  alkyl optionally substituted with one to three F, Cl, Br, I,

(d)  $C_3$ - $C_6$  cycloalkyl,

(e)  $-(C_1$ - $C_3$  alkyl)- $(C_3$ - $C_6$  cycloalkyl),

(f)  $(C_1$ - $C_6$  alkyl)-O- $(C_1$ - $C_3$  alkyl),

(g)  $C_2$ - $C_6$  alkenyl with one or two double bonds,

(h)  $C_2$ - $C_6$  alkynyl with one or two triple bonds,

(i)  $C_1$ - $C_6$  alkyl chain with one double bond and one triple bond,

(j)  $R_{1.4}$  aryl where  $R_{1.4}$  is as defined above, and

(k)  $R_{1.4}$  heteroaryl where  $R_{1.4}$  is as defined above,

- ~~(8)  $(CH_2)_{0-4}-CO-(C_1-C_{12}-alkyl)$ ,~~
- ~~(9)  $(CH_2)_{0-4}-CO-(C_2-C_{12}-alkenyl$  with one, two or three double bonds),~~
- ~~(10)  $(CH_2)_{0-4}-CO-(C_2-C_{12}-alkynyl$  with one, two or three triple bonds),~~
- ~~(11)  $(CH_2)_{0-4}-CO-(C_3-C_7-cycloalkyl)$ ,~~
- ~~(12)  $(CH_2)_{0-4}-CO-R_{1-ary1}$  where  $R_{1-ary1}$  is as defined above,~~
- ~~(13)  $(CH_2)_{0-4}-CO-R_{1-heteroary1}$  where  $R_{1-heteroary1}$  is as defined above,~~
- ~~(14)  $(CH_2)_{0-4}-CO-R_{1-heterocyclo}$  where  $R_{1-heterocyclo}$  is as defined above,~~
- ~~(15)  $(CH_2)_{0-4}-CO-R_{N-4}$  where  $R_{N-4}$  is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homethiomorpholinyl, homethiomorpholinyl S-oxide, homethiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of  $C_1-C_6$ -alkyl,~~
- ~~(16)  $(CH_2)_{0-4}-CO-O-R_{N-5}$  where  $R_{N-5}$  is selected from the group consisting of:~~
- ~~(a)  $C_1-C_6$ -alkyl,~~
- ~~(b)  $(CH_2)_{0-2}-(R_{1-ary1})$  where  $R_{1-ary1}$  is as defined above,~~
- ~~(c)  $C_2-C_6$ -alkenyl containing one or two double bonds,~~
- ~~(d)  $C_2-C_6$ -alkynyl containing one or two triple bonds,~~
- ~~(e)  $C_3-C_7$ -cycloalkyl, and~~
- ~~(f)  $(CH_2)_{0-2}-(R_{1-heteroary1})$  where  $R_{1-heteroary1}$  is as defined above,~~
- ~~(17)  $(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are as defined above,~~

- ~~(18)  $(CH_2)_{0-4}SO(C_1-C_6\text{-alkyl})$ ,~~
- ~~(19)  $(CH_2)_{0-4}SO_2(C_1-C_6\text{-alkyl})$ ,~~
- ~~(20)  $(CH_2)_{0-4}SO_2(C_3-C_7\text{-cycloalkyl})$ ,~~
- ~~(21)  $(CH_2)_{0-4}N(H\text{ or }R_{N-5})COOR_{N-5}$  where  $R_{N-5}$  can be the same or different and is as defined above,~~
- ~~(22)  $(CH_2)_{0-4}N(H\text{ or }R_{N-5})CON(R_{N-5})_2$  where  $R_{N-5}$  can be the same or different and is as defined above,~~
- ~~(23)  $(CH_2)_{0-4}NCON(R_{N-5})_2$  where  $R_{N-5}$  can be the same or different and is as defined above,~~
- ~~(24)  $(CH_2)_{0-4}N(H\text{ or }R_{N-5})COR_{N-5}$  where  $R_{N-5}$  and  $R_{N-3}$  can be the same or different and are as defined above,~~
- ~~(25)  $(CH_2)_{0-4}NR_{N-1}R_{N-3}$  where  $R_{N-1}$  and  $R_{N-3}$  can be the same or different and are as defined above,~~
- ~~(26)  $(CH_2)_{0-4}R_{N-4}$  where  $R_{N-4}$  is as defined above,~~
- ~~(27)  $(CH_2)_{0-4}OOC(C_1-C_6\text{-alkyl})$ ,~~
- ~~(28)  $(CH_2)_{0-4}OP(O)(OR_{N-aryl-1})_2$  where  $R_{N-aryl-1}$  is H or  $C_1-C_4\text{-alkyl}$ ,~~
- ~~(29)  $(CH_2)_{0-4}OCON(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,~~
- ~~(30)  $(CH_2)_{0-4}OCSN(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,~~
- ~~(31)  $(CH_2)_{0-4}O(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,~~
- ~~(32)  $(CH_2)_{0-4}O(R_{N-5})_2COOH$  where  $R_{N-5}$  is as defined above,~~
- ~~(33)  $(CH_2)_{0-4}S(R_{N-5})_2$  where  $R_{N-5}$  is as defined above,~~
- ~~(34)  $(CH_2)_{0-4}O(C_1-C_6\text{-alkyl optionally substituted with one, two, three, four, or five of F})$ ,~~
- ~~(35)  $C_3-C_7\text{-cycloalkyl}$ ,~~

~~(36) C<sub>2</sub>-C<sub>6</sub>-alkenyl with one or two double bonds optionally substituted with C<sub>1</sub>-C<sub>3</sub>-alkyl, F, Cl, Br, I, OH, SH, C≡N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub>-alkoxy, and NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,~~

~~(37) C<sub>2</sub>-C<sub>6</sub>-alkynyl with one or two triple bonds optionally substituted with C<sub>1</sub>-C<sub>3</sub>-alkyl, F, Cl, Br, I, OH, SH, C≡N, CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub>-alkoxy, and NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,~~

~~(38) (CH<sub>2</sub>)<sub>0-4</sub> N(H or R<sub>N-5</sub>) SO<sub>2</sub> R<sub>N-2</sub> where R<sub>N-5</sub> and R<sub>N-2</sub> can be the same or different and are as described above, or~~

~~(39) (CH<sub>2</sub>)<sub>0-4</sub> C<sub>3</sub>-C<sub>4</sub>-cycloalkyl,~~

~~(C) R<sub>N-aryl</sub>-W-R<sub>N-aryl</sub>,~~

~~(D) R<sub>N-aryl</sub>-W-R<sub>N-heteroaryl</sub>,~~

~~(E) R<sub>N-aryl</sub>-W-R<sub>N-1 heterocycle</sub> where R<sub>N-heterocycle</sub> is the same as R<sub>1-heterocycle</sub>,~~

~~(F) R<sub>N-heteroaryl</sub>-W-R<sub>N-aryl</sub>,~~

~~(G) R<sub>N-heteroaryl</sub>-W-R<sub>N-heteroaryl</sub>,~~

~~(H) R<sub>N-heteroaryl</sub>-W-R<sub>N-1 heterocycle</sub> where R<sub>N-1 heterocycle</sub> is the same as R<sub>1-heterocycle</sub>,~~

~~(I) R<sub>N-heterocycle</sub>-W-R<sub>N-aryl</sub>,~~

~~(J) R<sub>N-heterocycle</sub>-W-R<sub>N-heteroaryl</sub>,~~

~~(K) R<sub>N-heterocycle</sub>-W-R<sub>N-1 heterocycle</sub>,~~

~~where W is~~

~~(1) (CH<sub>2</sub>)<sub>0-4</sub>,~~

~~(2) O,~~

~~(3) S(O)<sub>0-2</sub>,~~

~~(4) N(R<sub>N-5</sub>) where R<sub>N-5</sub> is as defined~~

~~above, or~~

~~(5) CO,~~

where R<sub>C</sub> is:

(I)  $-C_3-C_{10}$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-OC(=O)NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-S(=O)_{0-2}R_{1-a}$  where  $R_{1-a}$  is as defined above,  $-NR_{1-a}C(=O)NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  $-C(=O)NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above, and  $-S(=O)_2NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

Al (II)  $-(CH_2)_{0-3}-(C_3-C_8)$  cycloalkyl where cycloalkyl can be optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O$ -phenyl,  $-CO-OH$ ,  $-CO-O-(C_1-C_4)$  alkyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(III)  $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$  where  $R_{C-x}$  and  $R_{C-y}$  are

$-H$ ,

$C_1-C_4$  alkyl optionally substituted with one or two

$-OH$ ,

$C_1-C_4$  alkoxy optionally substituted with one, two,

or three of

$-F$ ,

$-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl,

$C_2-C_6$  alkenyl containing one or two double bonds,

$C_2-C_6$  alkynyl containing one or two triple bonds,

or

phenyl,

and where  $R_{C-x}$  and  $R_{C-y}$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, -SO<sub>2</sub>-, -NR<sub>N-2</sub>- and  $R_{C-aryl}$  is the same as  $R_{N-aryl}$ ;

(IV) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub> is the same as  $R_{N-heteroaryl}$  and  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(V) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub>-R<sub>C-aryl</sub> where R<sub>C-aryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VI) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-aryl</sub>, R<sub>C-heteroaryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VII) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub>-R<sub>C-aryl</sub> where R<sub>C-heteroaryl</sub>, R<sub>C-aryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(VIII) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heteroaryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(IX) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-aryl</sub>-R<sub>C-heterocycle</sub> where R<sub>C-aryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above, and R<sub>C-heterocycle</sub> is the same as  $R_{N-heterocycle}$ ,

(X) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heteroaryl</sub>-R<sub>C-heterocycle</sub> where R<sub>C-heteroaryl</sub>, R<sub>C-heterocycle</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XI) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heterocycle</sub>-R<sub>C-aryl</sub> where R<sub>C-heterocycle</sub>, R<sub>C-aryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XII) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heterocycle</sub>-R<sub>C-heteroaryl</sub> where R<sub>C-heterocycle</sub>, R<sub>C-heteroaryl</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIII) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heterocycle</sub>-R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,

(XIV) - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>-R<sub>C-heterocycle</sub> where R<sub>C-heterocycle</sub>,  $R_{C-x}$  and  $R_{C-y}$  are as defined above,



(XV) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to  $R_C$ -aryl or  $R_C$ -heteroaryl or  $R_C$ -heterocycle where  $R_C$ -aryl or  $R_C$ -heteroaryl or  $R_C$ -heterocycle are as defined above where one carbon of cyclopentyl, cyclohexyl, or -cycloheptyl is optionally replaced with NH,  $NR_{N-5}$ , O,  $S(=O)_{0-2}$ , and where cyclopentyl, cyclohexyl, or -cycloheptyl can be optionally substituted with one or two  $-C_1-C_3$  alkyl, -F, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy, =O, or  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XVI)  $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$  where  $R_{C-1}$  and  $R_{C-2}$  are the same or different and are selected from the group consisting of:

(A) -H,

(B)  $-C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy, -O-phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(C)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy, -O-phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(C)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy, -O-phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(D)  $-(C_1-C_4 \text{ alkyl})-R_C\text{-aryl}$  where  $R_C\text{-aryl}$  is as defined for  $R_{1-aryl}$ ,

(E)  $-(C_1-C_4 \text{ alkyl})-R_C\text{-heteroaryl}$  where  $R_C\text{-heteroaryl}$  is as defined above,

(F)  $-(C_1-C_4 \text{ alkyl})-R_C\text{-heterocycle}$  where  $R_C\text{-heterocycle}$  is as defined above,

(G)  $-R_C\text{-heteroaryl}$  where  $R_C\text{-heteroaryl}$  is as defined above,

(H)  $-R_C\text{-heterocycle}$  where  $R_C\text{-heterocycle}$  is as defined above, and

(I)  $-R_{C'}\text{-aryl}$  where  $R_{C'}\text{-aryl}$  is as defined above, and where  $R_{C-3}$  is the same or different and is:

(A)  $-H$ ,

(B)  $-C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O\text{-phenyl}$ , and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(C)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl,

(D)  $-(C_1-C_4 \text{ alkyl})-R_{C'}\text{-aryl}$  where  $R_{C'}\text{-aryl}$  is as defined above,

(E)  $-(C_1-C_4 \text{ alkyl})-R_C\text{-heteroaryl}$  where  $R_C\text{-heteroaryl}$  is as defined above, or

(F)  $-(C_1-C_4 \text{ alkyl})-R_C\text{-heterocycle}$  where  $R_C\text{-heterocycle}$  is as defined above; or  
pharmaceutically acceptable salts thereof.

2. (Currently Amended) A substituted amine according to claim 1

where  $R_1$  is:

~~$-(CH_2)_{0-4}-(R_1\text{-aryl})$ , or~~

~~$-(CH_2)_{0-4}-(R_1\text{-heteroaryl})$~~

~~where  $R_1$  is:~~

~~\_\_\_\_\_  $R_{N-1}-X_N$  where  $X_N$  is selected from the group consisting of:~~

~~\_\_\_\_\_  $CO$ , and~~

~~\_\_\_\_\_  $SO_2$ ,~~

~~\_\_\_\_\_ where  $R_{N-1}$  is selected from the group consisting of:~~

~~\_\_\_\_\_  $R_{N-aryl}$ , and~~

~~\_\_\_\_\_  $R_{N-heteroaryl}$~~

where  $R_C$  is:

-C<sub>3</sub>-C<sub>8</sub> alkyl,

-(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl,

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub>-R<sub>C-aryl</sub>,

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub>-R<sub>C-heteroaryl</sub>,

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub>-R<sub>C-heterocycle</sub>, or

-cyclopentyl or -cyclohexyl ring fused to R<sub>C-aryl</sub> or R<sub>C-</sub>

heteroaryl or R<sub>C-heterocycle</sub>.

3. (Currently Amended) A substituted amine according to claim 2

where  $R_1$  is:

-(CH<sub>2</sub>)<sub>0-3</sub>-(R<sub>1-aryl</sub>), or

~~\_\_\_\_\_ (CH<sub>2</sub>)<sub>0-3</sub>-(R<sub>1-heteroaryl</sub>)~~

where  $R_2$  is -H;

where  $R_3$  is -H;

~~where  $R_N$  is:~~

~~\_\_\_\_\_  $R_{N-1}-X_N$  where  $X_N$  is:~~

~~\_\_\_\_\_  $CO$ ,~~

~~\_\_\_\_\_ where  $R_{N-1}$  is selected from the group consisting of:~~

~~\_\_\_\_\_  $R_{N-aryl}$ , and~~

~~\_\_\_\_\_  $R_{N-heteroaryl}$~~

where  $R_C$  is:

- (CH<sub>2</sub>)<sub>0-3</sub> - (C<sub>3</sub>-C<sub>7</sub>) cycloalkyl,
- (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub> - R<sub>C</sub>-aryl,
- (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub> - R<sub>C</sub>-heteroaryl,
- (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub> - R<sub>C</sub>-heterocycle, or
- cyclopentyl or -cyclohexyl ring fused to a R<sub>C</sub>-aryl or

R<sub>C</sub>-heteroaryl or R<sub>C</sub>-heterocycle.

4. (Original) A substituted amine according to claim 3  
where R<sub>C</sub> is:

- A1
- (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub> - R<sub>C</sub>-aryl,
  - (CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>1-4</sub> - R<sub>C</sub>-heteroaryl, or
  - cyclopentyl or -cyclohexyl ring fused to a R<sub>C</sub>-aryl or

R<sub>C</sub>-heteroaryl or R<sub>C</sub>-heterocycle.

5. (Cancelled)

6. (Original) A substituted amine according to claim 1  
where R<sub>1</sub> is

- (CH<sub>2</sub>) - (R<sub>1</sub>-aryl) where R<sub>1</sub>-aryl is phenyl substituted with two -  
F.

7. (Original) A substituted amine according to claim 6  
where the -F substitution is 3,5-difluorobenzyl.

8. (Original) A substituted amine according to claim 1  
where R<sub>2</sub> is -H.

9. (Original) A substituted amine according to claim 1  
where R<sub>3</sub> is -H.

10. (Currently Amended) A substituted amine according to claim 1 where  $R_N$  is  
 ~~$R_{N-1}-X_N$  where  $X_N$  is CO, where  $R_{N-1}$  is  $R_{N-aryl}$  where  $R_{N-aryl}$  is~~  
phenyl substituted with one  $-CO-NR_{N-2}R_{N-3}$  where the substitution on  
the phenyl is 1,3-.

11. (Original) A substituted amine according to claim 10  
where  $R_{N-2}$  and  $R_{N-3}$  are the same and are  $C_3$  alkyl.

Al 12. (Currently Amended) A substituted amine according to  
claim 1 where  $R_N$  is

~~$R_{N-1}-X_N$  where  $X_N$  is CO, where  $R_{N-1}$  is  $R_{N-aryl}$  where  $R_{N-aryl}$  is~~  
phenyl substituted with one  $C_1$  alkyl and with one  $-CO-NR_{N-2}R_{N-3}$   
where the substitution on the phenyl is 1,3,5-.

13. (Original) A substituted amine according to claim 12  
where  $R_{N-2}$  and  $R_{N-3}$  are the same and are  $C_3$  alkyl.

14. (Cancelled)

15. (Cancelled)

16. (Original) A substituted amine according to claim 1  
where  $R_C$  is:

- $(CR_{C-x}R_{C-y})_{1-4}-R_{C-aryl}$  where  $R_{C-aryl}$  is phenyl,
- $(CR_{C-x}R_{C-y})_{1-4}-R_{C-heteroaryl}$ , or
- cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-}$   
heteroaryl or  $R_{C-heterocycle}$ .

17. (Original) A substituted amine according to claim 16 where  $R_C$  is:  $-(CR_C-xR_C-y)_{1-4}-R_C$ -aryl where  $R_C$ -aryl is phenyl.

18. (Original) A substituted amine according to claim 17 where phenyl is substituted in the 3-position or 3,5-positions.

19. (Original) A substituted amine according to claim 16 where  $R_C$  is:

-  $(CH_2)-R_C$ -heteroaryl.

AI 20. (Original) A substituted amine according to claim 16 where  $R_C$  is:

-  $(CH_2)-R_C$ -heterocycle.

21. (Original) A substituted amine according to claim 16 where  $R_C$  is:

-cyclohexyl ring fused to a phenyl ring.

22. (Original) A substituted amine according to claim 1 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycolylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric,

dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

23. (Original) A substituted amine according to claim 1 which is selected from the group consisting of:

$N^1$ -[(1S,2S)-1-(3,5-difluorobenzyl)-3-(hexylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,

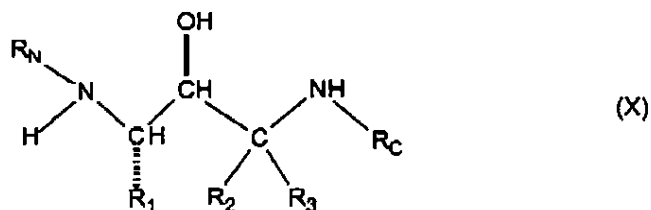
$N^1$ -[(1S,2S)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,

$N^1$ -[(1S,2S)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide, and

$N^1$ -(1S,2S)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide.

24. (Original) A method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's

disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound selected from the group consisting of a substituted amine of formula (X)



Al  
where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1, and pharmaceutically acceptable salts thereof.

25. (Original) A method of treatment according to claim 24 where the disease is Alzheimer's disease.

26. (Original) A method of treatment according to claim 24 where the method is helping prevent or delay the onset of Alzheimer's disease.

27. (Original) A method of treatment according to claim 24 where the disease is mild cognitive impairment.

28. (Original) A method of treatment according to claim 24 where the disease is Down's syndrome.

29. (Original) A method of treatment according to claim 24 where the disease is Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type.



30. (Original) A method of treatment according to claim 24 where the disease is cerebral amyloid angiopathy.

31. (Original) A method of treatment according to claim 24 where the disease is degenerative dementias.

32. (Original) A method of treatment according to claim 24 where the disease is diffuse Lewy body type of Alzheimer's disease.

33. (Original) A method of treatment according to claim 24 where the method is treating an existing disease.

34. (Original) A method of treatment according to claim 24 where the method is preventing a disease from developing.

35. (Original) A method of treatment according to claim 24 where the therapeutically effective amount for oral administration is from about 0.1 mg/day to about 1,000 mg/day; for parenteral, sublingual, intranasal, intrathecal administration is from about 0.5 to about 100 mg/day; for depo administration and implants is from about 0.5 mg/day to about 50 mg/day; for topical administration is from about 0.5 mg/day to about 200 mg/day; for rectal administration is from about 0.5 mg to about 500 mg.

36. (Original) A method of treatment according to claim 35 where the therapeutically effective amount is for oral administration is from about 1 mg/day to about 100 mg/day and for parenteral administration is from about 5 to about 50 mg daily.

37. (Original) A method of treatment according to claim 36 where the therapeutically effective amount for oral administration is from about 5 mg/day to about 50 mg/day.

38. (Original) A method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound selected from the group consisting of:

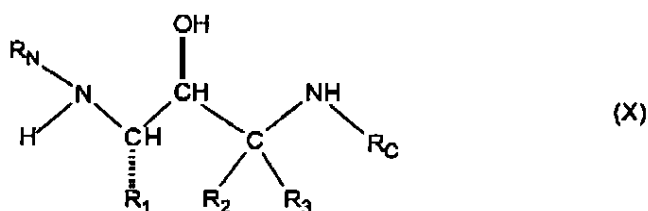
N<sup>1</sup>-[(1S,2S)-1-(3,5-difluorobenzyl)-3-(hexylamino)-2-hydroxypropyl]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

N<sup>1</sup>-[(1S,2S)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

N<sup>1</sup>-[(1S,2S)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide, and

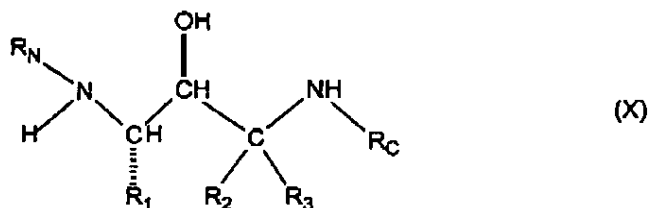
N<sup>1</sup>-(1S,2S)-1-(3,5-difluorobenzyl)-2-hydroxy-3-([(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propyl)-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide; and  
a pharmaceutically acceptable salt thereof.

39. (Original) A pharmaceutical composition which comprises a substituted amine of formula (X)



where R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>N</sub> and R<sub>C</sub> are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof, and a  
pharmaceutically acceptable diluent or carrier.

40. (Original) A method for inhibiting beta-secretase activity, comprising exposing said beta-secretase to an effective inhibitory amount of a compound of formula (X)



where R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>N</sub> and R<sub>C</sub> are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof.

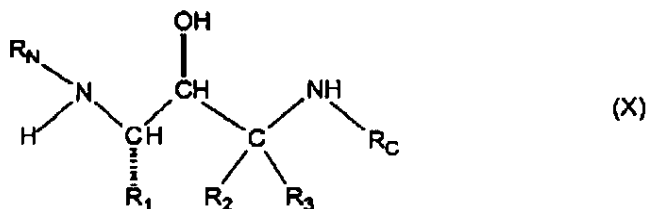
41. (Original) The method of claim 40, wherein said beta-secretase is exposed to said compound in vitro.

42. (Original) The method of claim 40, wherein said beta-secretase is exposed to said compound in a cell.

43. (Original) The method of claim 42, wherein said cell is in an animal.

44. (Original) The method of claim 43, wherein said animal is a human.

45. (Original) A method for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, comprising exposing said reaction mixture to an effective inhibitory amount of a compound of formula (X)



where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

46. (Original) The method of claim 45, wherein said cleavage site is between Met652 and Asp653, numbered for the APP-751 isotype; between Met 671 and Asp 672, numbered for the

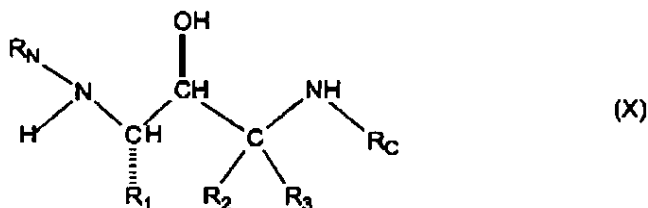
APP-770 isotype; between Leu596 and Asp597 of the APP-695 Swedish Mutation; between Leu652 and Asp653 of the APP-751 Swedish Mutation; or between Leu671 and Asp672 of the APP-770 Swedish Mutation.

47. (Original) The method of claim 45, wherein said reaction mixture is exposed *in vitro*.

48. (Original) The method of claim 47, wherein said reaction mixture is exposed in a cell.

Al 49. (Original) The method of claim 48, wherein said cell is a human cell.

50. (Original) A method for inhibiting production of amyloid beta peptide (A beta) in a cell, comprising administering to said cell an effective inhibitory amount of a compound of formula (X)

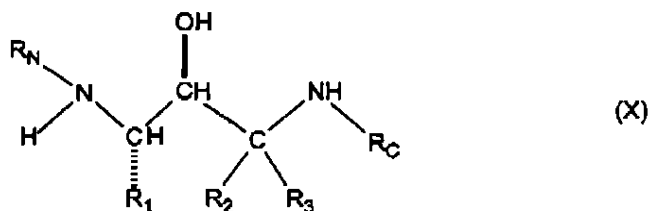


where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

51. (Original) The method of claim 50, wherein said administering is to an animal.

52. (Original) The method of claim 51, wherein said administering is to a human.

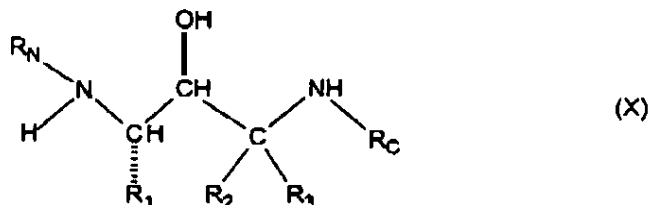
53. (Original) A method for inhibiting the production of beta-amyloid plaque in an animal, comprising administering to said animal an effective inhibitory amount of a compound of formula (X)



where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

54. (Original) The method of claim 53, wherein said animal is a human.

55. (Original) A method for treating or preventing a disease characterized by beta-amyloid deposits in the brain comprising administering to a patient an effective therapeutic amount of a compound of formula (X)



where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof.

56. (Original) The method of claim 55, wherein said therapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

57. (Currently Amended) The method of claim 55, wherein said ~~therapeutic~~ therapeutic amount is in the range of from about 15 to about 1500 mg/day.

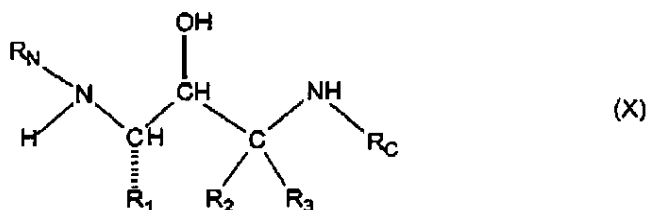
A1  
58. (Currently Amended) The method of claim 57, wherein said ~~therapeutic~~ therapeutic amount is in the range of from about 1 to about 100 mg/day.

59. (Currently Amended) The method of claim 58, wherein said ~~therapeutic~~ therapeutic amount is in the range of from about 5 to about 50 mg/day.

60. (Original) The method of claim 55, wherein said disease is Alzheimer's disease.

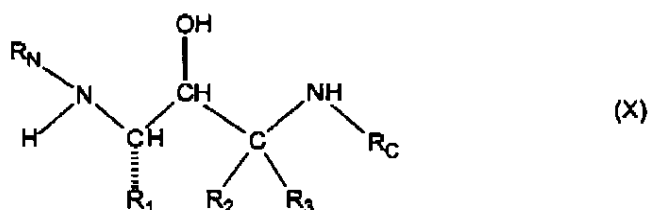
61. (Original) The method of claim 55, wherein said disease is Mild Cognitive Impairment, Down's Syndrome, or Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type.

62. (Original) A composition comprising beta-secretase complexed with a compound of formula (X)



where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof.

63. (Original) A method for producing a beta-secretase complex comprising: exposing beta-secretase, in a reaction mixture under conditions suitable for the production of said complex, to a compound of formula (X)



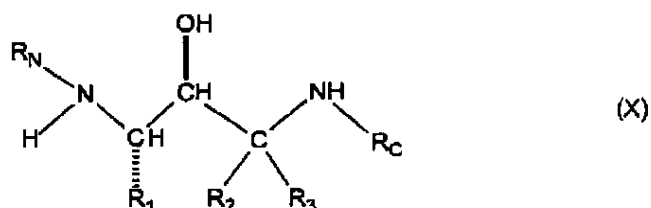
where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof.

64. (Original) The method of claim 63, where said exposing is *in vitro*.

65. (Original) The method of claim 63, wherein said reaction mixture is a cell.



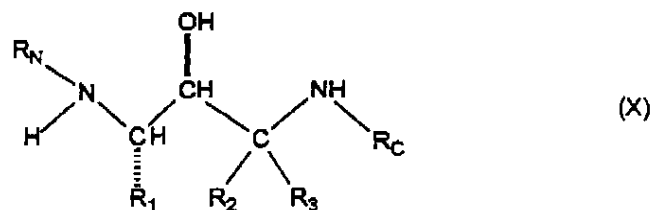
66. (Original) A kit comprising component parts capable of being assembled, wherein at least one component part comprises, enclosed in a container, a compound of formula (X)



AI  
where R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>N</sub> and R<sub>c</sub> are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

67. (Original) The kit of claim 66, wherein said compound is lyophilized and at least one further component part comprises a diluent.

68. (Original) A kit comprising a plurality of containers, each container comprising one or more unit dose of a compound of formula (X)



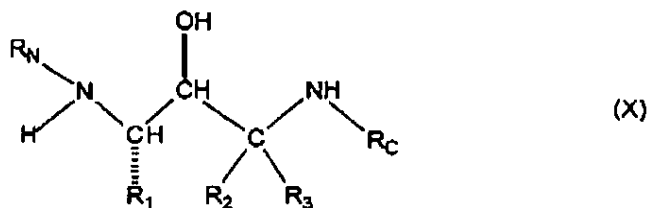
where R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>N</sub> and R<sub>c</sub> are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

69. (Original) The kit of claim 68, wherein each container is adapted for oral delivery and comprises a tablet, gel, or capsule.

70. (Currently Amended) The kit of claim 69, wherein each container is adapted for ~~parenteral~~ parenteral delivery and comprises a depot product, syringe, ampoule, or vial.

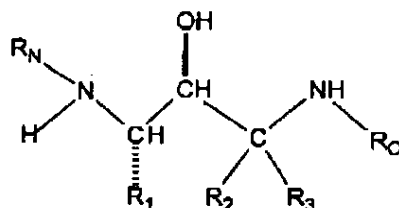
71. (Original) The kit of claim 69, wherein each container is adapted for topical delivery and comprises a patch, medipad, ointment, or cream.

A1  
72. (Currently Amended) A kit comprising one or more therapeutic agent selected from the group consisting of an antioxidant, an ~~anti-inflammatory~~, anti-inflammatory, a gamma secretase inhibitor, a neurotrophic agent, an acetylcholinesterase inhibitor, a statin, an A beta peptide, and an anti-A beta antibody; and  
a compound of formula (X)



where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof.

73. (Original) A composition comprising an inert diluent or edible carrier; and  
a compound of formula (X)

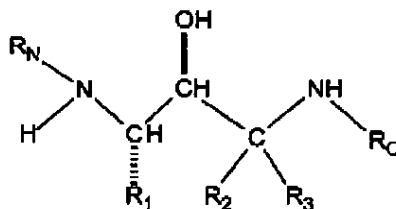


(X)

where R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>N</sub> and R<sub>C</sub> are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof.

74. (Original) The composition of claim 73, wherein said  
carrier is an oil.

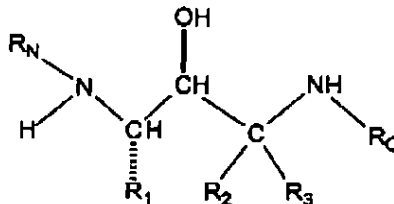
Al 75. (Original) A composition comprising a binder,  
excipient, disintegrating agent, lubricant, or gildant; and  
a compound of formula (X)



(X)

where R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>N</sub> and R<sub>C</sub> are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof..

76. (Original) A composition comprising a compound of  
formula (X)



(X)

A1 where  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_N$  and  $R_C$  are as defined in claim 1,  
or a pharmaceutically acceptable salt thereof,  
and where the compound is disposed in a cream, ointment, or  
patch.